REMARKS

Applicants respectfully request consideration of the following reasons upon continued examination of the present application on the merits.

I. Status of the Claims

Claims 1-26, 51-53 and 107-109 were cancelled previously. Claims 27 and 56 are amended to correct a typographical error (correcting "immuriological' to "immunological"; the correct spelling is recited in claim 87). It is acknowledged that the amendments are made after final rejection of the claims. However, because the amendments do not introduce new matter, and because they either place the application in condition for allowance or at least in better condition for appeal, entry thereof is respectfully requested. Claims 27-50 and 87-106 are pending, with claims 54-86 and 110-111 withdrawn from consideration.

II. Rejection of Claims under 35 U.S.C. §102(e)

Claims 27-35, 37-50, 87-94, and 96-106 are rejected under 35 U.S.C. §102(e) for alleged anticipation by U.S. Patent No. 6,395,300 to Straub et al. ("Straub"). Applicants respectfully traverse the rejection.

The rejection is made under 35 U.S.C. §102(e) because the reference dated May 27, 1999 does not constitute a statutory bar against the present application, which benefits from a priority date of May 18, 2000.

On the strength of the accompanying Rule 1.131 Declaration executed by co-inventor Stephen Ruddy, Applicants have demonstrated that the claimed invention was reduced to practice by the inventors prior to May 27, 1999, which is the earliest priority date of Straub. Swearing behind a reference only requires a prior reduction to practice of a single embodiment within the scope of the claimed invention. *See* MPEP 715.02, which states that "[t]he 37 C.F.R. §1.131 affidavit or declaration must established possession of either the whole invention claimed

or something falling within the claim (such as a species of a claimed genus), in the sense that the claim as a whole reads on it." Therefore, the contents of the declaration submitted herewith meet the requirements for a 37 C.F.R. §1.131 affidavit or declaration.

Accordingly, Straub is disqualified as citable art against the present application. Applicants respectfully requests withdrawal of the rejection.

III. Rejection of Claims under 35 U.S.C. §103(a)

A. Straub

The Examiner states that claims 36 and 95 are rejected under 35 U.S.C. §102(e) for alleged anticipation by Straub. However, this rejection is listed under the heading of "Claim Rejections – 35 U.S.C. §103(a)," and the Examiner expressly acknowledges that "[t]he teaching of Straub differs from the instant invention in the specific average particle size of the active agent, namely less than about 50 nm." Therefore, Applicants presume that the Examiner intended to reject claims 36 and 95 under 35 U.S.C. §103(a) and respectfully traverse the rejection.

As stated in the foregoing section, Straub is disqualified as cited art against the claimed invention. Accordingly, Applicants respectfully request withdrawal of the rejection.

B. Eickhoff, Straub, and Acosta-Cuello

Claims 27-50 and 87-106 are rejected under 35 U.S.C. §103(a) for allegedly being obvious over U.S. Patent No. 5,518,738 to Eickhoff et al. ("Eickhoff") in view of Straub, and further in view of Applicants' allegedly admitted prior art of record or PCT Publication No. WO 97/18796 by Acosta-Cuello et al. ("Acosta-Cuello"). Applicants respectfully traverse the rejection.

(i) "Rapid onset" and "rapid disintegration" are not equivalent.

The Examiner asserts that "Eickhoff teaches a rapidly-acting ('more rapid onset of action') solid oral dose form" and expressly acknowledges that "Eickhoff is silent about the preparation of said composition into matrix or porous matrix form." Final Office Action, the paragraph bridging pages 6 and 7.

The alleged "rapidly-acting" composition of Eickhoff is not equivalent to the claimed oral solid dose rapidly disintegrating nanoparticulate active agent formulation which also has a rapid onset of action. This is because "rapid onset" (meaning a quick start of the therapeutic action of the drug") cannot be equated with, and is not the same as, "rapid disintegration" (meaning fast melt of the drug dosage form). There is no necessary correlation between rapid onset and rapid disintegration, as discussed in the specification, excerpted below:

> *. . . While prior art fast melt dosage forms may provide rapid presentation of a drug, frequently there is an undesirable lag in the onset of therapeutic action because of the poor solubility and associated slow dissolution rate of the drug. Thus, while prior art fast melt dosage forms may exhibit rapid disintegration of the drug carrier matrix, this does not result in rapid dissolution and absorption of the poorly soluble drug contained within the dosage form.*

Specification, page 4, last paragraph. As repeatedly argued in the prior response, the claimed invention is distinguishable from prior art in that the claimed invention achieved rapid onset via increasing bioavailability of the drug by formulating the drug into a nanoparticulate drug composition, as well as a rapidly disintegrating dosage form by integrating the nanoparticulate drug composition into a solid dose porous matrix which dissolves upon contact with saliva in less than about 3 minutes.

(ii) Straub is disqualified as cited art.

Straub, which is cited for the alleged teaching of a porous matrix form, is disqualified as citable art under 35 U.S.C. §103(a). For this reason alone, the rejection should be withdrawn.

(iii) Neither the specification nor Acosta-Cuello teaches or suggests a rapidly disintegrating dosage form of a nanoparticulate active agent composition, as the Examiner asserts.

Additionally, Applicants emphasize that the specification is **not** admitted prior art, as the Examiner asserts. According to the Examiner, "Applicant's admitted prior art of record and WO'796 [Acosta-Cuello] are provided as supplemental references to demonstrate the routine knowledge in preparing micro- or nano-particulate compositions in a rapidly disintegrating or dissolving or fast-melting solid oral dose or matrix form" (final Office Action, page 7, last paragraph).

Acosta-Cuello fails to teach a rapidly disintegrating formulation of ***a nanoparticulate active agent composition***, as evidenced by the paragraph pinpoint cited by the Examiner and reproduced below:

> *A solid dosage form according to a preferred embodiment of the present invention is a compressed tablet suitable for ingestion. The expression "pharmaceutical active ingredient" as used in this disclosure means a drug, vitamin or mineral. Drugs may include, without limitation, antacids, antibiotics, antiseptics, antiulcerative agents, analgesics, antihistamines, antivirals, antiparasitic drugs, laxatives, gastro-intestinal motility modifying agents, antinauseants, antihyperlipidaemic agents, anti-inflammatories, antidiuretics, antiflatulents, tranquilizers, stimulants,sedatives, antihypertensives, anticonvulsants, antiepileptics, oncologic therapy, decongestants, antiasthmatics, betablockers and combinations thereof. In a most preferred embodiment, the pharmaceutical active ingredient comprisded in the solid dosage form is an antacid or a mixture of antacids. However, the present invention is not intended to be strictly limited to antacids as active ingredients.*

Moreover, as previously submitted, nowhere does the specification admit that a rapidly disintegrating formulation of a nanoparticulate active agent composition is prior art. Rather, Applicants submitted the Ruddy Declaration to attest to the fact that one skilled in the art would not have any reason to combine rapidly disintegrating technology with nanotechnology to obtain the claimed invention.

The Examiner simply dismissed the declaration evidence by stating that "taste-masking technique. . . is not necessarily implemented in the preparation of a rapidly disintegrating or dissolving or 'fast melt' dosage form." Final Office Action, page 14, lines 3-5. However, isolated instances that some fast melt dosage forms do not require film coating (for example, some drugs do not have the unpleasant taste that requires taste masking) do not change the general principal of drug formulation. Accordingly, Applicants respectfully request that the Examiner give proper weight to Applicants' rebuttal evidence in determining patentability of the claimed invention.

In view of the foregoing, Applicants respectfully request withdrawal of the rejection.

IV. Double Patenting Rejection

A. U.S. Patent No. 6,165,506

Claims 27-50 and 87-106 are rejected under the judicially created doctrine of double patenting over claims 1-16 and 21 of U.S. Patent No. 6,165,506 ("the '506 patent") in view of Applicants' allegedly admitted prior art of record or Straub. Applicants respectfully traverse the rejection.

The claims of the '506 patent are directed to a solid dose nanoparticulate naproxen formulation comprising, *inter alia*, a pharmaceutically acceptable alkali agent, which functions to increase the dissolution rate of the drug matrix surrounding the nanoparticulate naproxen in the solid dose formulation. There is no reason that one skilled in the art would have included a pharmaceutically acceptable alkali agent in the claimed invention because there is no evidence on the record that the alkali agent would increase the dissolution rate of any drug other than naproxen. Although the present claims recite the open-ended transitional phrase "comprising," the Examiner is not at the liberty to read additional claim limitations into the claims, which would alter the features of the claimed invention, and which is not even disclosed in the present specification.

Accordingly, the '506 patent does not teach or suggest the claimed invention. Straub is disqualified as citable art. Accordingly, Applicants respectfully request withdrawal of the rejection.

B. U.S. Patent No. 7,276,249

Claims 27-50 and 87-106 are rejected under the judicially created doctrine of double patenting over claims 1-177 of U.S. Patent No. 7,276,249 ("the '249 patent) in view of Applicants' allegedly admitted prior art of record, PCT Publication No. WO 01/45674 by Kerkhof et al. ("Kerkhof") or Straub. Applicants respectfully traverse the rejection.

The '249 patent relates to a nanoparticulate fibrate composition. Straub is not citable art. Neither the specification nor Kerkhof discloses a rapidly disintegrating dosage form of a nanoparticulate active agent composition. In fact, in the prior response, Applicants submitted the Ruddy Declaration to demonstrate that one skilled in the art would not have considered it obvious to combine conventional rapidly disintegrating technology with nanotechnology. Accordingly, Applicants respectfully request that the Examiner withdraw the rejection.

CONCLUSION

The present application is now in condition for allowance. Favorable reconsideration of the application as amended is respectfully requested. The Examiner is invited to contact the undersigned by telephone if it is felt that a telephone interview would advance the prosecution of the present application.

The Commissioner is hereby authorized to charge any additional fees which may be required regarding this application under 37 C.F.R. §§ 1.16-1.17, or credit any overpayment, to Deposit Account No. 19-0741. Should no proper payment be enclosed herewith, as by the credit card payment instructions in EFS-Web being incorrect or absent, resulting in a rejected or incorrect credit card transaction, the Commissioner is authorized to charge the unpaid amount to

Deposit Account No. 19-0741. If any extensions of time are needed for timely acceptance of papers submitted herewith, Applicants hereby petition for such extension under 37 C.F.R. §1.136 and authorizes payment of any such extensions fees to Deposit Account No. 19-0741.

Respectfully submitted,

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By /Yang Tang/

FOLEY & LARDNER LLP
Customer Number: 31049
Telephone: (202) 672-5538
Facsimile: (202) 672-5399

Michele M. Simkin
Attorney for Applicant
Registration No. 34,717

Yang Tang
Attorney for Applicant
Registration No. 55,663